NEURONAL MECHANISMS OF FOOD PERCEPTION

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To my husband.

Contents

1 Publications of the thesis

CHAPTER 3: SEEING FOOD

Blechert J, Meule A, Busch NA, **Ohla K** (2014). *Food-pics: an image database for experimental research on eating and appetite.* **Frontiers in Psychology**, 5:617

Meindl M, **Ohla K** (2015). *Die Farbe macht den Geschmack - Farbwirkung in der Nahrungswahrnehmung.* **Ernährungsumschau**. 62(3):163-169. *Review*

Toepel U, **Ohla K**, Hudry J, le Coutre J, Murray M M (2014). *Verbal labels selectively bias brain responses to high-energy foods.* **Neuroimage**, 87:154–163.

CHAPTER 4: TASTING FOOD

Ohla K, Busch NA, Lundström JN (2012). *Time for taste–a review of the early cerebral processing of gustatory perception.* **Chemosensory Perception**, 5(1):87–99. *Review*

Ohla K, Hudry J, le Coutre J (2009). *The cortical chronometry of electrogustatory event–related potentials.* **Brain Topography**, 22(2):73–82

Ohla K, Toepel U, Johannes le Coutre, and Julie Hudry (2010). *Electrical neuroimaging reveals intensity dependent activation of human cortical gustatory and somatosensory areas by electric taste.* **Biologial Psychology**, 85(3):446–455

Crouzet SM, Busch NA, **Ohla K** (2015). *Taste quality decoding parallels taste sensations.* **Current Biology**. 25(7):890-896

Ohla K, Toepel U, le Coutre J, Hudry J (2012). *Visual-gustatory interaction: orbitofrontal and insular cortices mediate the effect of high-calorie visual food cues on taste pleasantness.* **PloS ONE**, 7(3):e32434

Seubert J, **Ohla K** (2012). *A dynamic cortical network encodes violations of expectancy during taste perception.* **The Journal of Neuroscience**, 32(6): 1918-1919. *Review*

CHAPTER 5: FOOD FLAVOR

Seubert J, **Ohla K**, Yokomukai Y, Kellermann T, Lundström JN (2015). *Superadditive opercular activation to food flavor is mediated by enhanced temporal and limbic coupling*. **Human Brain Mapping**, 36(5):1662-76

2 Introduction and Background

In Western societies, people are faced with an omnipresence of food. Particularly palatable and energy-rich snacks and fast-food seem available wherever we go. Researchers partially attribute rising obesity rates and problems in eating-related self-regulation to this factor (Meule and Vögele, 2013; Morris et al., 2014). In fact, it becomes more and more difficult for consumers to make the "right" or "healthy" choice as health and nutritional claims on food products and in the media draw a partially biased, incomplete, confusing or even false picture of what constitutes a healthy diet and how far the product contributes to health and well-being. Besides, in modern societies the main purpose of eating has long shifted away from the maintenance of homeostatic needs (De Castro et al., 2010) and eating has become a means for social interaction and a source of pleasure making it even more strenuous to follow a strict dietary regimen. Furthermore, a blunted response and/or sensitivity of the reward system to food as a consequence of overeating may further stimulate eating beyond physiological needs and promote weight gain (Franken and Muris, 2005; Stice et al., 2008; Pandit et al., 2012). As a consequence, overweight and obesity rates are on a steady rise affecting about 52% of the world's population (World Health Organization, 2015) taking epidemic dimensions and posing an economic burden to society (De Castro et al., 2010).

What characterizes food and makes it so tempting? Sensory and hedonic information about food is conveyed by all senses, activated more or less simultaneously, having led to the notion that food perception is a multisensory experience (Verhagen and Engelen, 2006; de Araujo and Simon, 2009). The smell, sight, touch or sound of a food can be experienced before ingestion and elicit expectations about the "taste" of that food based on previous encounters. It is, therefore, not surprising that these so-called pre-ingestive sensory experiences play a role in the formation of cravings and the elicitation of appetitive responses (Hardman et al., 2014; Mela, 2001).

Consciously or unconsciously, we constantly sample our environment for cues to make predictions about upcoming events based on prior experiences and learned associations (Helmholtz, 1910). This is also true for food; expectations about sensory properties and reward aspects of food are effortlessly elicited by everyday experiences such as the smell or sight of a food or the label on a package. Imagine the smell of fresh baked croissants which suggest, first of all, their availability but also allow make predictions about sensory properties, such as the butteriness, and affective properties, such as the pleasure, regret or guilt associated with the consumption (or restraint). Expectations about upcoming sensory events bias perception toward the anticipated events, leading to facilitated (expedited) processing when expectations are met, while perception is impeded when expectations are violated (Veldhuizen et al., 2011b). Veldhuizen et al. (2011b) give a memorable example: "For example, one can imagine accidentally sipping a fine Chardonnay while expecting water. The sensation of the wine would be surprising and likely lead to the immediate halting of ingestion. Such a response, though negating the chance to savor fine Chardonnay, makes evolutionary sense because incorrect decisions to swallow can incur dire consequences." (p. 14735).

Only during consumption, the chemical senses, smell, taste and oral touch and irritation, are experienced in the oral cavity as food is masticated and swallowed (see Simon et al., 2006) and gives rise to the overall experience commonly referred to as *taste*. While the term *taste* is, strictly speaking, incorrect

as it does not refer to the gustatory perception, many languages including German lack an appropriate term for the holistic *flavor* experience arising from the food-induced stimulation of the chemical senses, gustation, olfaction and oral somatosensation (Lawless and Lee, 1993) in a minimalist interpretation, or, in a broader sense, of all our senses, including hearing and vision (Verhagen and Engelen, 2006). It is important to note that *flavor* is a perceptual construct or *Gestalt* resulting from the merging of food-related sensory information at the brain level (Small, 2012). *Flavor* often extends beyond the mere addition of the unimodal sensory modalities involved, being usually perceived as more object-like, intense and rewarding compared to its constituents.

Undoubtedly, feeding behavior is characterized by a complex interplay of perceptual, cognitive and metabolic processes and research on the mechanisms by which these processes regulate food intake behavior is only in its infancy. In this thesis, I will focus on the perceptual basis of food choice, the cortical representations of the visual, gustatory and flavor aspects of food and their susceptibility to contextual information.

CHAPTER 3 will briefly introduce the role of the visual encounter of food in food perception and appetite (see Meindl and Ohla, 2015, for an overview on the role of food color). Here, the importance of stimulus control in studies on food viewing will be emphasized and a controlled food image database (Blechert et al., 2014) will be presented. The chapter will close with an example of how expectations elicited by verbal cues impact visual food processing (Toepel et al., 2014), a topic that has received only little attention so far. Despite its special role in the recognition of the nutritional content or potential toxicity of food, the sense of taste has been largely neglected by neuroscientific and psychological research. I will, therefore, give a comprehensive introduction on gustatory perception in CHAPTER 4. I will introduce the neural workings of human taste perception and present a series of studies characterizing the spatiotemporal properties of taste processing (Ohla et al., 2009, 2012a) and the neural representations of the most pertinent taste features, taste intensity (Ohla et al., 2010), taste quality (Crouzet et al., 2015) and taste hedonics (Ohla et al., 2012b). The latter will also serve to illustrate the susceptibility of taste perception to contextual information and the expectations thereof (Seubert and Ohla, 2012). In CHAPTER 5, I will demonstrate the perceptual consequences and neural representations when taste and smell merge and form flavor during consumption of a beverage (Seubert et al., 2015) to emphasize the singularity and relevance of flavor in food perception .

3 Seeing food

The sight of food is among the first sensory impressions contributing to food perception. It constitutes an integral part of the anticipatory phase of food perception as the visual appearance elicits expectations about other sensory and hedonic attributes of a food thereby impacting food choice markedly. How would an advertising for chocolate muffins on your way to the cafeteria influence your choice of lunch? The encoding and integration of low level visual features (Treisman and Gelade, 1980; Ashby et al., 1996) together with top-down influences (Fenske et al., 2006; Trapp and Bar, 2015) are the foundations of object categorization and identification. Semantic categorization of food, in contrast to other object categories, goes beyond objective schemes such as *food versus nonfood* or *fruits versus vegetables*. Food categories can likewise be based on subjective and emotional schemes like *preferred versus*

unpreferred or *delicious versus disgusting* as well as schemes that require proficient knowledge about nutrition and health consequences such as energy-density, macronutrient content, etc. In line with the view that food object categories are complex, human neuroimaging studies revealed that visual food categorization involves large-scale brain networks that extend well beyond visual cortical areas.

To examine the factors underlying appetitive responses to foods, images have been commonly used in laboratory studies, mostly for convenience reasons because they are easier to control and apply than real foods. There is evidence that the mere viewing of food images activates brain areas related to taste perception, reward processing and decision-making (Killgore et al., 2003; Wagner et al., 2012; Schur et al., 2009; Grimm et al., 2012). This is not surprising because visual food cues elicit expectations about the pre-ingestive availability and palatability of food and represent conditioned stimuli associated with food ingestion (Dagher, 2012). Particularly, the posterior fusiform gyrus, the left lateral orbitofrontal cortex and the left middle insula respond to visual food contrasted to nonfood objects as revealed in a recent meta-analysis (van der Laan et al., 2011). Responses to food images are susceptible to physiological states of hunger as measured for implicit food evaluation (Seibt et al., 2007; Hoefling and Strack, 2008), salivation (Wooley and Wooley, 1981), visual attention processing (Stockburger et al., 2009), autonomic responding (Rodriguez et al., 2005), and reward activity (Uher et al., 2006), particularly in the right amygdala and left lateral orbitofrontal cortex (van der Laan et al., 2011).

Food viewing provides a promising tool to study food perception and attitudes toward food as well and it has, in fact, proven a valid approach, for example, to distinguish individuals with deviant eating behavior and healthy controls. Inter-individual differences in food image processing have been reported for example for restraint (Blechert et al., 2010), external (Nijs et al., 2009) or emotional (Bohon et al., 2009) eaters as well as obese subjects (Nijs and Franken, 2012) compared to healthy controls. Yet, also healthy individuals with normal eating behavior exhibited gender-related differences in brain responses to food images, particularly in brain areas associated with valuation and food intake control (Toepel et al., 2012). Food viewing tasks have been, therefore, adapted to train eating control, for example, in food-specific inhibition tasks (van Koningsbruggen et al., 2014) with measurable effects on actual food intake corroborating the notion that responding to food images is causally involved in eating behavior.

3.1 Image features influence visual food perception

van der Laan et al. (2011) noted in their meta-analysis that "the results [of the studies included] are heterogeneous and there still is uncertainty about the core brain regions involved in the neural processing of viewing food pictures" leaving open whether methodological differences between studies, for example the choice of stimulus material, contributed to the observed inter-study variations. Notably, the stimulus material varies across studies and images are seldomly made available to other researchers thereby rendering across-laboratory comparisons and replications difficult. In order to allow for across-laboratory compatibility of research findings, databases of well-characterized images for experimental research on food perception and eating behavior have been established recently (Foroni et al., 2013; Blechert et al., 2014). The databases were designed to allow custom compilations of image material driven by specific research questions or target populations, e.g., food items that 20-40 year old women desire to eat or food and control items of a given complexity, color or size. The databases are available to researchers and will hopefully increase across studies.

While the database by Foroni et al. (2013) (Foodcast Research Image Database,*FRIDa*) provides a heterogeneous selection of images, it contains only a few edible food items, typically consumed in the Mediteranean diet, and the normative data is derived from a small sample (N=73) which questions their generalizability. The *Food.pics* database (Blechert et al., 2014), in contrast, comprises a more balanced collection of 883 photographs of food objects, food-related objects (e.g., kitchen utensils) and non-food control items. Considering edible foods only, it covers various food categories including fruits, vegetables, meat, fish, beverages, candy, dairy, food packages, meals, snack food and raw food items representative of typical foods in western countries (see Figure 1). The images of both databases are well characterized in terms of the most pertinent physical features including color, size, brightness, within-object contrast, complexity and spatial frequencies. When selecting images, for example of food and nonfood items, users are able to compare and match physical images features and thereby minimize confounds from differences in the physical appearance, which affects neuronal responses but also behavior (Knebel et al., 2008; Willenbockel et al., 2010; Foroni et al., 2013). Food color, for example, plays an important role in food perception and valuation. Color is an apparent and often even a diagnostic features of food objects; it can indicate ripeness (e.g., a yellow versus a green banana) and edibility (e.g., grey food is mostly moldy). Color undoubtedly plays a crucial role in food hedonic perception and the guidance of food choice (see Meindl and Ohla, 2015; Spence, 2015, for recent reviews).

Macronutrient content (e.g., fat, protein or sugar), on the other hand, are less obvious food properties. Yet, at the brain level, images of low and high caloric foods are distinguishable. Calorie-related differences have been reported in cortical areas associated with object perception and decision-making within less than 200 ms following presentation of the food images suggesting that the visual detection of high energy food occurs automatic (Toepel et al., 2009). Moreover, images of high-energy foods are less prone to response adaptation than images of low-energy foods (Lietti et al., 2012). These findings suggest that the visual encounter of food allows, at least a coarse, categorization according to energy content at a glimpse. The ability to evaluate food before ingestion with respect to energy and macronutrient content may subserve the maintenance of energy homeostasis and guide food choice. In light of these findings, visually presented foods must be controlled for macronutrient content (proteins, carbohydrates, fat), portion size as well as energy density (see Blechert et al. (2014)).

Finally, internal factors such as food habits and attitudes toward food but also current physiological states influence food perception, particularly food deprivation renders high-energy foods more palatable (Goldstone et al., 2009). While habits and attitudes are not readily accessible within time-constraint surveys, the state variables hunger and current dieting were obtained from the participants who evaluated the images of the *Food.pics* database Blechert et al. (2014) according to perceptual and psychological parameters: familiarity, recognizability, complexity, valence, arousal, and for items only, desire to eat and palatability by a large sample (N=1988) spanning a wide range of age (11–77 years), BMI (12–67 kg/m^2), and cultural background (German-speaking countries and the USA), to provide robust and generalizable normative data.

3.2 Expectation influences visual food perception

Food perception is not only influenced by imminent features of the food itself but also implicit and explicit external cues impact perception and subsequent decisions. In the food context, verbal labels,

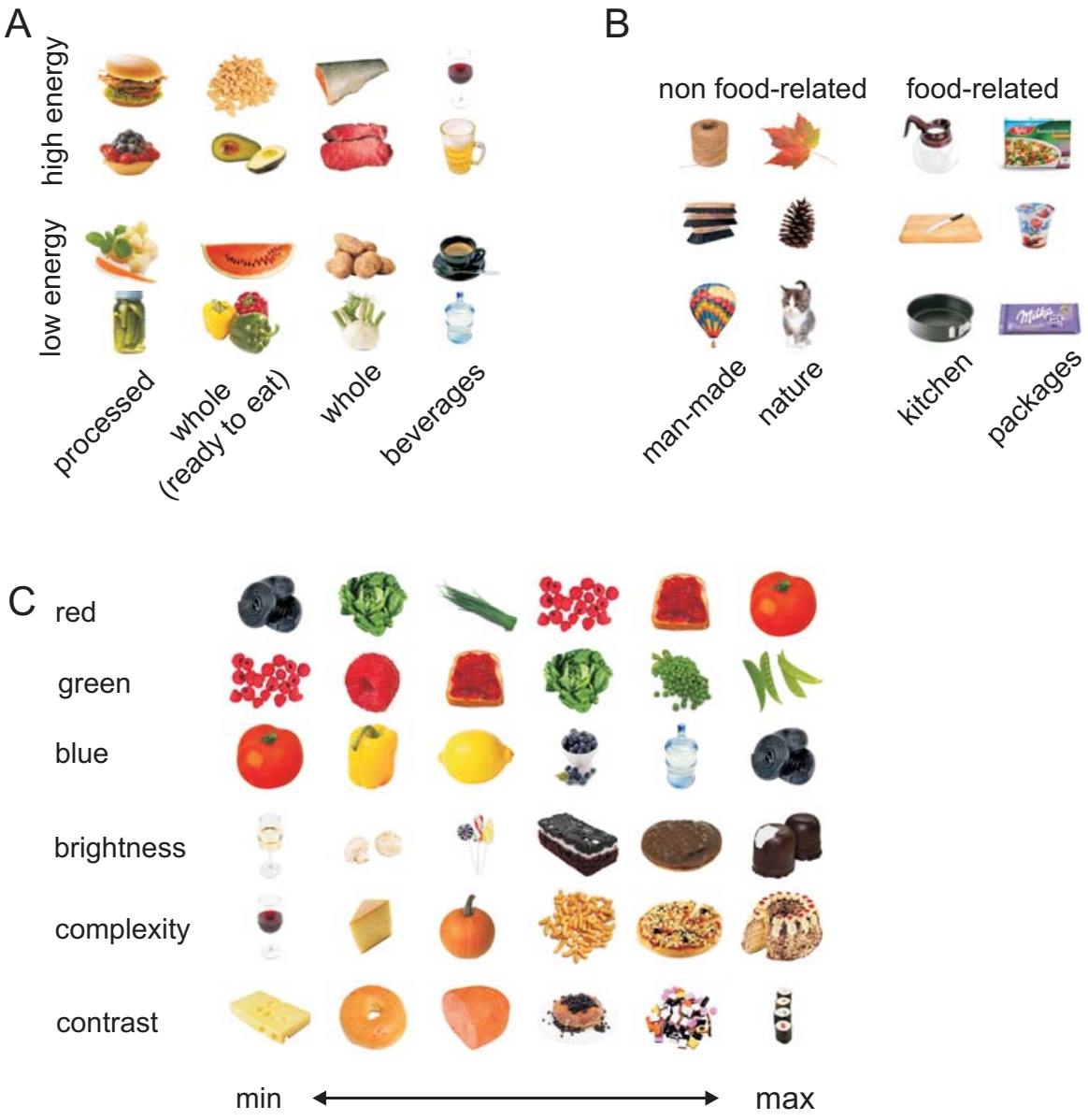

Figure 1: Food photographs from the *Food.pics* database (Blechert et al., 2014) can be selected and grouped according to various aspects such as energy density and degree of processing (A). The database comprises images of food-related objects such as kitchen utensils and food packages as well as non-edible natural and man-made control objects (B). Each image is accompanied with measures of physical properties including RGB-color, brightness, complexity and contrast (C).

as can be found on any food product, have been shown to influence the perception and valuation food stimuli across the senses. For example, positive compared to neutral labels increase the reported pleasantness of taste and flavor stimuli (Grabenhorst and Rolls, 2008). Similarly, pleasant labels reduce the experienced negative valence of otherwise unpleasant odors (de Araujo et al., 2005). In both studies, the changes in subjective experience toward more positive or less negative were accompanied by increased activity in the medial orbitofrontal cortex consistent with its role in the processing of reward value. Food labels inform about a food's composition, origin, potential health consequences, etc. and thereby help consumers in the process of food decision making and food choice (see Melissa G. Bublitz, 2010). The powerful effects of labels can, in part, be attributed to halo effects. Lee et al. (2013) demonstrated only recently how positive attributes of organic production transfer to food sensory and hedonic attributes: their participants reported that food with labels implying "organic" production tastes better, contains less fat and more fibers then the same food when "conventionally" produced. Linder et al. (2010) showed that "organic" labels activate brain areas related to reward perception stronger compared to the same food items without label. Labels related to nutrient content have been repeatedly shown to influence food categorization at the behavioral and brain response level (Killgore et al., 2003; Toepel et al., 2009; van der Laan et al., 2011). Toepel et al. (2009) have shown that images of high- versus low-energy foods were processed differentially even when the energy density was task irrelevant pointing to an automatic and implicit categorization which is in line with the proposed motivational salience of high-calorie food (Frank et al., 2010).

Understanding the mechanisms by which labels influence food perception and food choice is critical to tackle deviant eating behavior and thereby reduce detrimental health consequences for individuals in the long run. Specifically, prior imaging studies left open whether verbal labels influence early, sensory or later, evaluative aspects of food perception. This question was addressed in a recent study (Toepel et al., 2014). The authors investigated how verbal labels varying along the valence dimension of emotion (positive, neutral, and negative) modulate the spatiotemporal brain processing of images displaying high- and low-energy foods using electroencephalography (EEG). Visual evoked potentials to high-energy food images were modulated by positive compared to neutral or negative labels over the 260–300 ms post-stimulus period and accompanied by reduced activity in brain areas associated with cognitive control and goal-adaptive behavior (posterior, frontal, insular and cingulate regions). The relatively late latency of the effect suggests that valence labels act upon the cognitive evaluation rather than the initial sensory analysis of the food object and is consistent with representing reduced cognitive control and increased valuation of the high-energy foods preceded by positive labels. Notably, responses to low-energy food images were unaffected by verbal valence cues entirely. The results indicate that the cortical network related to cognitive control and goal-adaptive behavior, which serves to prevent consumption beyond energy needs, is less efficient when, often unhealthy yet palatable, high-energy foods occur with positive valence cues. Future studies will have to show whether these findings indeed translate to increases in experienced reward, influence food choice and foster overconsumption of high-energy foods.

4 Tasting food

In most species, the sense of taste serves the distinction of potentially nutritious and harmful food ingredients. It is hence considered a gateway for the energy and nutrient balance and, as such, instrumental in

the selection, acceptance and rejection of food. The most intriguing questions in taste research concern the neuronal representations of the most pertinent features of taste: intensity, quality and valence.

The repertoire of taste perception is often described by and limited to so-called *basic* or *primary* taste qualities (Bartoshuk, 1988), which constitute defined, non-overlapping categories, salty, sweet, sour, bitter and umami. It should be noted, however, that these categories, root centuries back, evolved from the need to communicate about food efficiently (see Erickson, 2008), leaving unanswered whether the limited number of conventional verbal descriptors suffice to characterize our multifarious perceptual experiences. Erickson (2008) recently criticized the concept of basic tastes because "This concept of basic tastes has no rational definition to test, and thus it has not been tested" (p. 59). While a universal definition of basic tastes is indeed still lacking, some researchers refer to them with reference to Henning's proposition of a tetrahedral taste space with salty, sweet, sour and bitter tastes at the four corners (Henning, 1916). According to Henning (1916), the tetrahedral taste space allows to capture the entirety of taste experiences by the experiences reported along the axis connecting two basic tastes as he describes it "Dabei erlebe ich eine kontinuierliche Reihe einfacher Geschmäcke, in denen die Ähnlichkeit zum Ausgangsglied beim Fortschreiten nachlässt, während die Ähnlichkeit zum Endglied immer mehr wächst" (p. 212). The tetrahedron does, however, exclude the incorporation of additional basic tastes. While classical definitions of taste quality relied more on phenomenological experiences, researchers nowadays propose novel taste qualities upon discovery of specific taste receptors or receptor candidates.

Each quality has been proposed to serve maintenance of a physiological equilibrium. Accordingly, sweet taste signals the presence of energy in form of carbohydrates, salty taste suggests the availability of electrolytes, sour taste points to a low pH (e.g., from spoiled food or vitamin C) and bitter taste indicates potentially harmful or even toxic ingredients. Umami (delicious savory) taste became commonly accepted as the fifth quality after the discovery of the umami receptor (Chaudhari et al., 2000); umami taste has been associated with the detection of proteins. Although, umami alone is detectable and discriminable, at least with practice, it is not very palatable and yet potent to enhance salty taste. There is accumulating evidence for the existence of additional *primary* tastes including fat (Laugerette et al., 2005), calcium (Tordoff et al., 2012), and CO_2 (Fischler et al., 2007); each of these tastes could be serving a physiological equilibrium as well.

Undoubtedly, all organisms require efficient mechanisms for taste detection and identification to enable adaptive ingestion-related behavior (e.g., food rejection to prevent potential intoxication). Accordingly, most animals are able to detect tastes bearing nutritional and/or behavioral relevance (Chandrashekar et al., 2006) and humans can proficiently categorize prototypical substances representing basic tastes (Hettinger et al., 1999). In addition to taste quality, the strength or intensity of a taste influences food acceptance; for example, low to moderate levels of salt are appreciated in many foods, whereas oversalted foods most likely cause aversion and rejection. Both, taste quality and intensity conjointly influence taste hedonics or valence, which constitutes a pertinent, affective feature characterizing taste.

In contrast to the far senses vision, audition, and olfaction, gustation is only elicited at a short-range, i.e., upon ingestion in mammals (see Liman et al. (2014) for other species). Taste quality is encoded by specialized receptors, mostly on the tongue, which detect chemicals corresponding to each of the basic tastes (Chandrashekar et al., 2006) before the information is further transmitted via segregated neuronal

fibers (Chen et al., 2011), distributed coding across neuronal fibers (Pfaffmann, 1941; Erickson, 1963), or dynamic firing patterns (Katz et al., 2002) to the gustatory cortex in the insula.

How the peripheral signal is used by the human central nervous system to encode taste is only beginning to be understood. This is due, in part, to the fact that chemical stimuli delivered into the mouth are difficult to control with respect to their physical properties, i.e., place of stimulation and onset/offset. Most of our current understanding of the cortical areas involved in human taste perception has been derived from neuroimaging studies relying on haemodynamic measures which are relatively forgiving to imprecise stimulus onset such as functional magnetic resonance imaging (fMRI) or positron emission tomography (PET). These studies have revealed that liquid oral stimuli activate most frequently several subdivisions of the insula, the orbitofrontal cortex, and the anterior cingulate cortex (Kinomura et al., 1994; Zald et al., 1998; Frey and Petrides, 1999; Small et al., 1999; de Araujo et al., 2003a; Schoenfeld et al., 2004; Kringelbach et al., 2004). According to a recent meta-analysis of the available gustatory functional imaging papers (Veldhuizen et al., 2011a), a significant and widespread probability of activations was observed in the bilateral insula and the overlying opercula, the left lateral and right medial orbitofrontal cortex, and the pregenual cingulate cortex, indicating that these regions are reliably and consistently activated in response to gustatory stimulation. The human insula has indeed been associated with the sensory processing of taste features such as intensity (Grabenhorst and Rolls, 2008) and quality (Schoenfeld et al., 2004) and is often referred to as primary taste area. The orbitofrontal cortex, on the other hand, has been frequently linked to the processing of hedonic aspects of taste (Kringelbach et al., 2003; McCabe and Rolls, 2007) and is often referred to as secondary taste area.

4.1 Cortical taste processing

However, cortical activation patterns change rapidly, within the millisecond time range. Thus, the slow and aggregated hemodynamic measures acquired with fMRI and PET have clear and inherent problems with providing insights into the dynamics of the early cerebral processing of gustatory stimuli which are accessible using techniques with excellent temporal resolution such as electroencephalography (EEG). Event-related potentials (ERPs) are commonly used to characterize the cortical mechanisms underlying human perception and cognition. Although the first successful gustatory ERP recordings were reported almost half a century ago (Funakoshi and Kawamura, 1968; Plattig, 1969; Funakoshi and Kawamura, 1971) only a minuscule number of publications has emerged since. In a recent review, Ohla et al. (2012a) discussed 40 studies using EEG and Magnetoencephalography (MEG) on gustatory perception in humans. The low number of publications is surprising giving that the ERP technique is well established for other senses including olfaction; numerous reports describe the waveform of olfactory ERPs (Kobal and Hummel, 1988; Murphy et al., 1994; Evans et al., 1993; Pause et al., 1997), which exhibit a similar morphology to ERPs recorded from non-chemosensory stimulation with notable variations in the topographical distribution and time course, though.

As measuring ERPs requires a good summation of the evoked potential, in particular, stimuli must be unimodal, have a precise stimulus on- and offset time and have short rise and fall times with respect to its duration various taste delivery systems have been developed during the last decades, each of which met the requirements to evoke event-related potentials to greater or lesser extent. The first attempts to measure gustatory ERPs have been made using a hinged spoon to deliver the taste solutions,

which evoked a concomitant tactile potential (Funakoshi and Kawamura, 1971). Plattig (1969), at about the same time, used electrogustometry, i.e., electrical pulses applied to lingual taste bud fields, to elicit a peculiar perception referred to as electric taste; the electric stimulation introduced a markable electric artifact which obfuscated the gustatory ERP. Only 40 years later, the time course of a largely uncontaminated electrogustatory ERP has been shown after separation of the electrogustometric artifact from the neural portion of the EEG with independent component analysis (Ohla et al. (2009); see Figure 2 A). Dipole analysis revealed that the early components, P1 and N1, could be explained with generators in the bilateral insular cortices and the adjacent operculi, the areas comprising the primary taste cortex, suggesting that reported signal contains a gustatory component. While electrogustometry is a convenient means to control taste stimulation both, temporally and spatially, and is of clinical significance for the diagnostics of taste disturbances (Tomita and Ikeda, 2002), it elicits a unique taste experience that cannot readily be compared to the taste experiences associated with food.

Tactile-free delivery systems for flowing tastants have revolutionized taste research only recently and allowed electrophysiological studies to shed light on the dynamics of neuronal activation patterns elicited by naturalistic taste experiences (see Ohla et al. (2012a)). Kobayakawa and colleagues developed a protocol to combine flowing taste stimulation with MEG, EEG and SQUID measurements not only to localize the primary taste area but to also describe the temporal properties of cortical taste responses (Kobayakawa et al., 1996, 1999). For this, they designed a stimulation system that requires placement of a tube with a small incision placed on the tongue; suction resulting from the flow of liquids in the tube keeps the incision at place and allows the liquid stimulate a well defined area of the tongue. In this system, a taste solution is embedded in a constant flow of tasteless solution with a micro-air bubble in between the two liquids to prevent mixing or dilution. Taste research has already started to and will continue to profit from the commercial availability of a tactile-free spray gustometer that mimics constant flow through a regular stream of spray pulses delivered onto the protruded tongue. Here, the tastants are also embedded in a sequence of tasteless pulses thereby habituating the lingual somatosensory system and allowing a unimodal, gustatory stimulation (Singh et al., 2011; Tzieropoulos et al., 2013; Crouzet et al., 2015). Using these stimulation techniques, up to four consecutive ERP components (P1, N1, P2 and/or a late positivity) have been observed. For the first positive gustatory deflection, the P1, peak latencies around 130–150 ms for salt (Mizoguchi et al., 2002; Wada, 2005) and electric taste (Ohla et al., 2009, 2010) and early (80-130 ms) components obtained with MEG for salty and sour tastes (Kobayakawa et al., 1996; Mizoguchi et al., 2002; Onoda et al., 2005) have been consistently reported, although, early event-related potential deflections are not always described, probably because these transient deflections with steep flanks are particularly vulnerable to minuscule jitters in stimulus timing. When they are reported, however, they exhibit a similar morphometry and time course (see Figure 2). The P1 was localized to gustatory cortical areas and interpreted as a sensory component related to the processing of sensory taste features (Mizoguchi et al., 2002; Ohla et al., 2009, 2010); N1 and P2 were localized to various cortical structures in addition suggesting they represent higher order gustatory functions (see Figure 2 C).

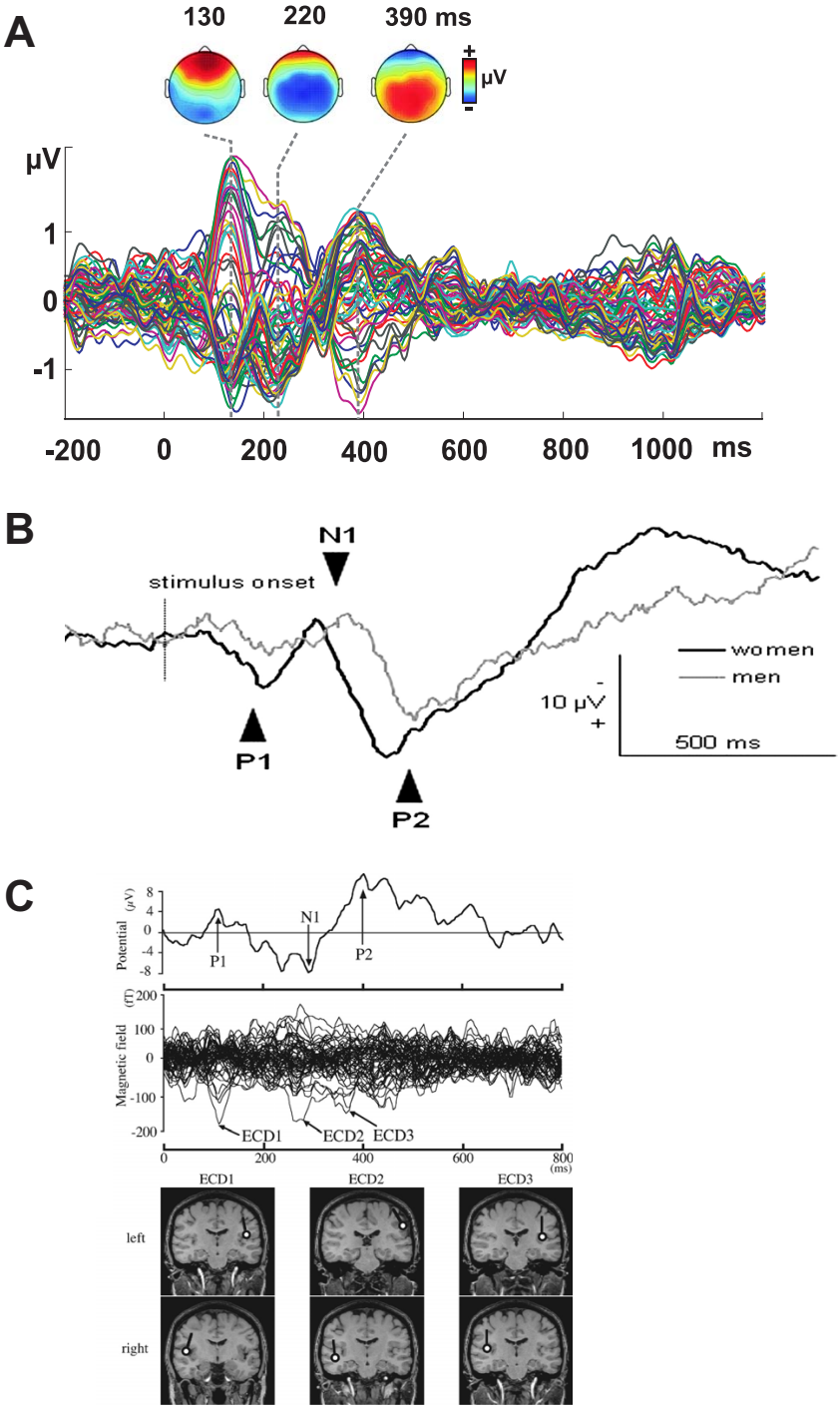

Figure 2: Event-related responses to electric taste, acetic acid, and salt solution exhibit a relatively similar event-related potential morphology. Note that the time scales have been matched and stimulus onset is at 0 ms. A: Event-related potentials to electric taste, from 64 electrodes, exhibit a frontal P130, a fronto-central N220, and a late centro-posterior P390 (Ohla et al., 2009). B: The event-related potential to acetic acid, from electrode Cz, shows four distinct components: P1 at 200 ms, N1 at 350 ms, P2 at 450 ms, and a late positive component. Notably women exhibited shorter latencies and larger amplitudes than men (Hummel et al., 2010). C: Three major components, at 104 ms (ECD1), at 292 ms (ECD2), and at 392 ms (ECD3), were observed from simultaneously recorded EEG (upper panel) and MEG (lower panel) in a single participant. Dipole modeling revealed the temporal dynamics of the cortical activations, which started in the bilateral insula/ operculum (ECD1), spread to the central sulcus and temporal cortex (ECD2), and returned to the bilateral insula (ECD3) within 400 ms (Mizoguchi et al., 2002). (Reproduced from Ohla et al., 2012a).

4.2 Taste intensity processing

Taste intensity perception contributes to the assessment of the relative concentration of a given food constituent such as sugar or salt and are a vital part of the sensory assessment of food. Increases in stimulus intensity commonly cause faster and stronger neuronal responses and thereby facilitate stimulus detection. Particularly early ERP components reflect changes in physical stimulus properties such as stimulus intensity in audition (Rapin et al., 1966), contrast in vision (Spekreijse et al., 1973) and concentration in olfaction (Pause et al., 1996; Tateyama et al., 1998). Likewise, changes in the concentration of tastants have been suggested to be signaled by the firing rate of taste-responsive cells (Scott and Perrotto, 1980; Ganchrow and Erickson, 1970), which would result in an amplitude increase of the evoked potential at the scalp. Indeed, an increase in anodal direct currents has been shown to reduce the onset latency of the intracortical field potentials with a concurrent increase in field potential amplitude in rats (Yamamoto et al., 1980). Similarly, increased activation of the primary taste cortex has been observed in human neuroimaging studies (Small et al., 2003; Spetter et al., 2010). Taste intensity-dependent shifts of the ERP waveform toward shorter latencies and higher amplitudes have been observed to acetic acid (Kobal, 1985), electric taste (Ohla et al., 2010), citric acids (Hummel et al., 2010), and salt (Tzieropoulos et al., 2013) though the effects occurred at varying latencies. However, reports of higher amplitudes without latency shift to NaCl and saccharin (Saito et al., 1998) exist as well. In line with the non-chemical senses, Tzieropoulos et al. (2013) found shorter behavioral response latencies to more intense stimuli and a positive relation between behavioral, response times, and neural response, ERP, latencies. In contrast, Saito et al. (1998) found no response time difference at the neuronal level but reported a speedup of behavioral responses to stronger tastes.

It is debated whether an increase in taste concentration can lead to concomitant activation of the oral somatosensory system via free nerve fibers innervating the tongue (Komiyama et al., 2007). In an attempt to disentangle the gustatory from the somatosensory component of the electric taste response, Ohla et al. (2010) compared event-related potentials to electric taste presented at individual taste threshold level, thereby exciting gustatory fibers selectively without concomitant excitation of trigeminal fibers, and at high intensity evoking a prickling sensation and, thus activating trigeminal fibers mainly. Because somatosensory but not gustatory potentials have been observed stronger over the contralateral hemisphere (Maloney et al., 2000; Bennett and Jannetta, 1980) taste stimulation was unilaterally applied to either the right or left side of the tip of the tongue. Sour, salty and metallic tastes were reported at both intensities while clear prickling and burning was reported at high intensity only. In line with the bulk of literature on non-chemosensory responses, overall increased amplitudes and shorter latencies of the event-related potential were observed for high as compared to low intensities. Surprisingly, the eERP waveform as well as the topographical distributions were otherwise highly similar suggesting that the ERPs to both intensities have the same neural origin. Reconstruction of the sources further corroborated this notion, at least in part: the initial P1 yielded a source in the bilateral taste areas in the anterior insula, superior temporal cortex and other areas at 70–80 ms consistent with a prior finding (Ohla et al., 2009). While the latency of this activation appears rather fast, it reflects unlikely a purely lingual somatosensory response as this would occur much earlier at latencies of around 10-60 ms and more pronounced over the contralateral hemisphere. The average current intensity used for taste stimulation was several-fold below the intensity needed to activate trigeminal fibers as shown in electrophysiological studies in ro-

dents (Pfaffmann, 1980; Bujas et al., 1979; Yamamoto et al., 1980) and clinical studies in humans (Bull, 1965). "However, trigeminal fibers convey not only tactile and thermal but also gustatory information and are also found in taste buds. There is evidence for a functional interaction between the gustatory and trigeminal systems, both at peripheral and central levels (Hanamori et al., 1997; Nomura and Ogawa, 1985; Boucher et al., 2003). Recent findings point to an overlap of the terminal fields of the trigeminal nerve and the chorda tympani in the gustatory nucleus of the solitary tract providing an "anatomical substrate for trigemino-gustatory interactions" (Felizardo et al., 2009). It is, thus, conceivable that gustatory and trigeminal afferents project to overlapping downstream cortical areas. This was confirmed by the present findings." (Ohla et al., 2010, p. 452-453).

4.3 Taste quality processing

Taste quality is encoded by specialized receptors on the tongue which detect chemicals corresponding to each of the basic tastes (sweet, salty, sour, bitter, and savory) before taste quality information is conveyed to the gustatory cortex in the insula(Chandrashekar et al., 2006). Studies of single neuron and neuronal population responses in rodents have provided evidence for different, but not necessarily exclusive, encoding schemes. According to the labeled lines theory, segregated lines are responsible for encoding a particular taste (Chen et al., 2011). However, the existence of broadly tuned gustatory neurons (Stapleton et al., 2006) also suggests a distributed coding across neuronal lines or fibers (Pfaffmann, 1959). Yet another dynamic models of taste coding suggest that dynamic firing patterns, signaling across fibers, carry taste information (Katz et al., 2002). This model is in fact most suitable to explain flexible, learning-dependent cortical taste representations when cortical activation patterns change with learning (Carleton et al., 2010). Although these approaches provide valuable information regarding the activity of individual neurons or small groups of neurons to a specific tastant, they usually do not allow investigations of the spatial and dynamic organization of neuronal activity at a macroscopic, whole-brain level with the exception of novel optical neuroimaging methods allowing the to monitor the neuronal activity of the entire gustatory cortex in vivo (Chen et al., 2011; Carleton et al., 2010; Accolla et al., 2007).

Furthermore, previous animal studies have focused on how the peripheral and central nervous systems respond to a given chemical. The neuronal signal obtained in response to a sensory stimulus cannot be readily associated with the resulting phenomenological experiences. However, preference and avoidance behavior has often been interpreted as an indirect measure of taste quality perception (Carleton et al., 2010); along these lines, avoidance behavior to a tastant of the alkaloid family may be interpreted as bitter taste experience. Human studies, on the other hand, can factor in also the perceptual dimension, that is the reported phenomenological taste experience. All three dimensions (chemical, neuronal and perceptual) can be described as an abstract representation or space in which distances correspond to similarity relations Haddad et al. (2008). "For example, in the neural space, each dimension corresponds to the activity of one neural unit or, as in our case, electrode. If two tastants evoke neural patterns that are close in neural space, their response patterns are similar. Likewise, two tastes that are close in perceptual space are expected to taste similar." (Crouzet et al., 2015, , p. 893-894). To date, very little is known about cortical taste representations and their relation to subjective taste perception and perceptual decision making. However, gustatory research must still elucidate how neuronal taste representations

are experienced and how they determine food-related decisions such as eating more of one food while rejecting another.

To address this question, Crouzet et al. (2015) combined EEG as a large-scale electrophysiological measure with behavioral reports of subjective taste quality experiences a) to test how, when, and where in the human brain taste quality information is represented and b) to show that these neural representations provide the previously unknown foundation for taste-related decision making. Participants tasted a salty, sweet, sour, or bitter solution and reported the experienced taste quality on each trial. Prominent taste-related differences in the neural signatures, i.e., the latencies, amplitudes as well as the spatial (topographical) scalp distributions of gustatory-evoked potentials indicate that taste qualities are distinctly represented in the brain. The authors applied time-resolved multivariate pattern classification analyses (MVPA) to the electroencephalogram to test whether the global neuronal response patterns based on all electrodes allowed to decipher which of four tastants participants tasted on a given trial (see Figure 3, A). Indeed, the classifiers accurately predicted which of four tastes was presented in a given trial suggesting that the large-scale neuronal response patterns carry information about taste quality (Figure 3, B) as it has been shown in electrophysiological studies in rodents for structures of the gustatory pathway such as the nucleus of the solitary tract Di Lorenzo et al. (2009), the parabrachial nucleus Geran and Travers (2013), and the gustatory cortex Jezzini et al. (2013).

For each taste, the onset of significant decoding coincided with the earliest taste-evoked responses, within only 175 ms, suggesting that quality is among the first attributes of a taste represented in the central gustatory system (see Figure 3, D). The early event-related responses have been commonly associated with the representation of sensory stimulus features in vision Busch et al. (2004), audition Rapin et al. (1966), olfaction Pause et al. (1997) as well as gustation (taste intensity) Ohla et al. (2010); Tzieropoulos et al. (2013). Accordingly, taste quality can be viewed a sensory stimulus feature. The cortical sources of the initial taste-evoked responses were localized to the insula and opercular cortices, areas that have been previously implicated in taste quality processing (Small, 2010; Kobayakawa et al., 1999; Veldhuizen et al., 2011a). Importantly, the authors excluded that differences in taste intensity and pleasantness, which are also processed in the insula Small et al. (2003); Nitschke et al. (2006), contributed to and confounded taste quality discrimination and, thereby, influenced decoding performance by showing that participants' ratings of pleasantness and intensity did not correlate with decoding performance. Furthermore, a relation between the neuronal response patterns and the reported subjective taste experience was demonstrated (Figure 3, C): "the more similar the multivariate response patterns of any two tastes were (and thus, the less a classifier could discriminate between them), the more these tastes were confused by the participants." (Crouzet et al., 2015, , p. 895) evidencing, for the first time, a neural-phenomenological mapping for taste quality. Future studies should further this approach to investigate whether different chemicals belonging to the same taste category (e.g., different alkaloids) elicit similar or distinct neural response pattern thereby probing the notion of categorical (in contrast to continuous) taste quality perception.

4.4 Taste hedonics and the role of expectations

Systematic investigations of taste hedonics without concomitant manipulation in taste quality or intensity are difficult to achieve because the different taste qualities exhibit large inter-individual variability in liking

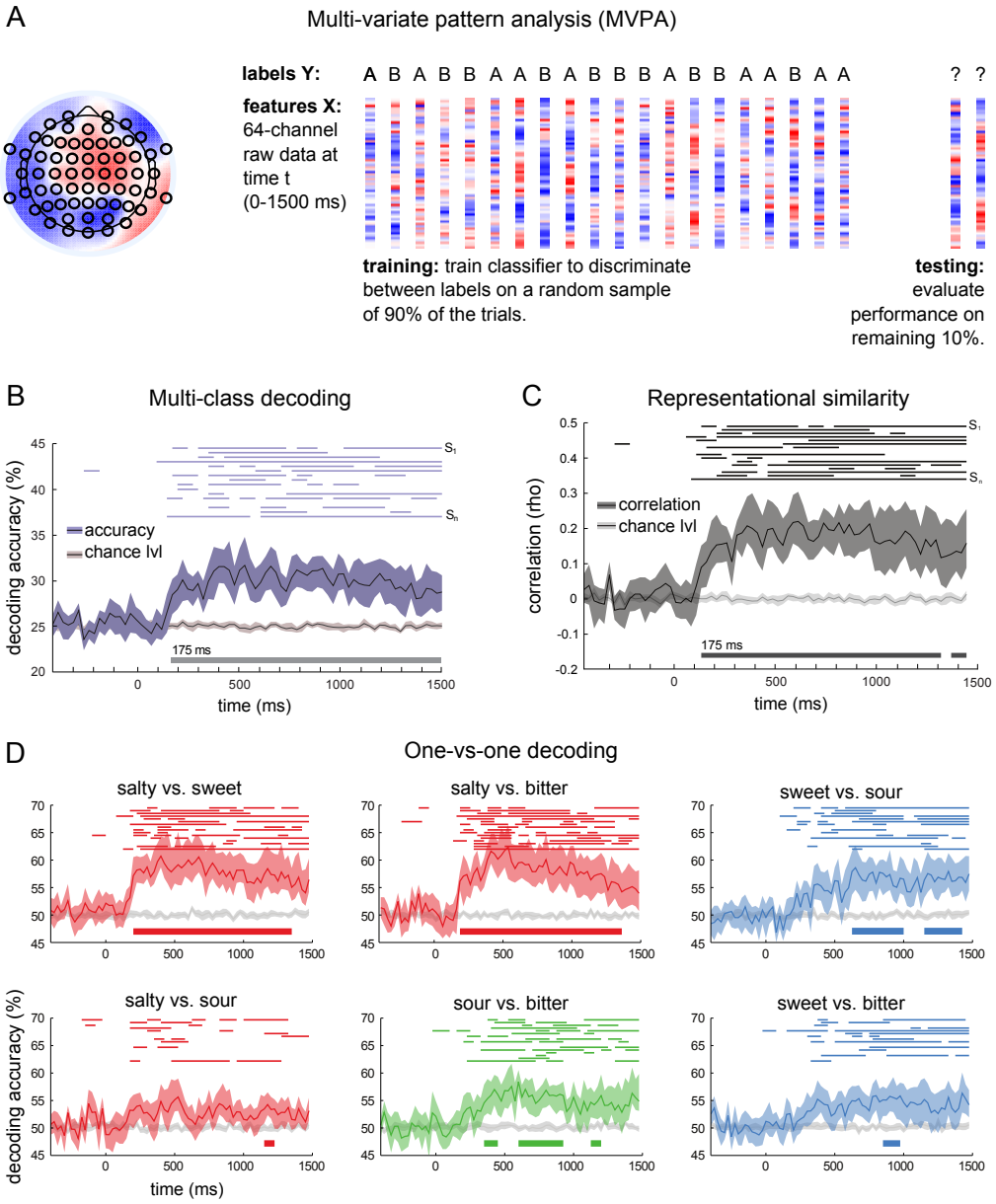

Figure 3: Multivariate pattern analysis (MVPA) yielded significant decoding starting at 175 ms and a close relation to the pattern of errors of the participants. A) For a given participant and time point, a random sample of 90% of the trials was used to train a classifier to discriminate between brain responses (EEG scalp topography) associated with two (one-versus-one classification) or four (multiclass discrimination) tastants. Classification performance was then evaluated by using the remaining 10% of the trials. The entire procedure was repeated for 120 cross-validations. B) Multi-class decoding: classifiers were trained to provide at each time point an answer to the question: "Which taste is this?". The black curve indicates decoding accuracy averaged across participants (shaded area: bootstrapped 95% confidence interval; light gray curve: average chance level). The thin (top) and thick (bottom) horizontal lines correspond to the period of significant decoding for individual participants, and at the group level, respectively. C) Representational similarity analysis: behavioral confusion matrices were correlated with neural confusion matrices at each time point to estimate the similarity between taste representations in perceptual space and in neuronal space. Conventions as in B. D) One-vs-one decoding: classifiers were trained to provide at each time point an answer to the question: "Is this taste X or taste Y?". Conventions as in B. (Reproduced from Crouzet et al., 2015).

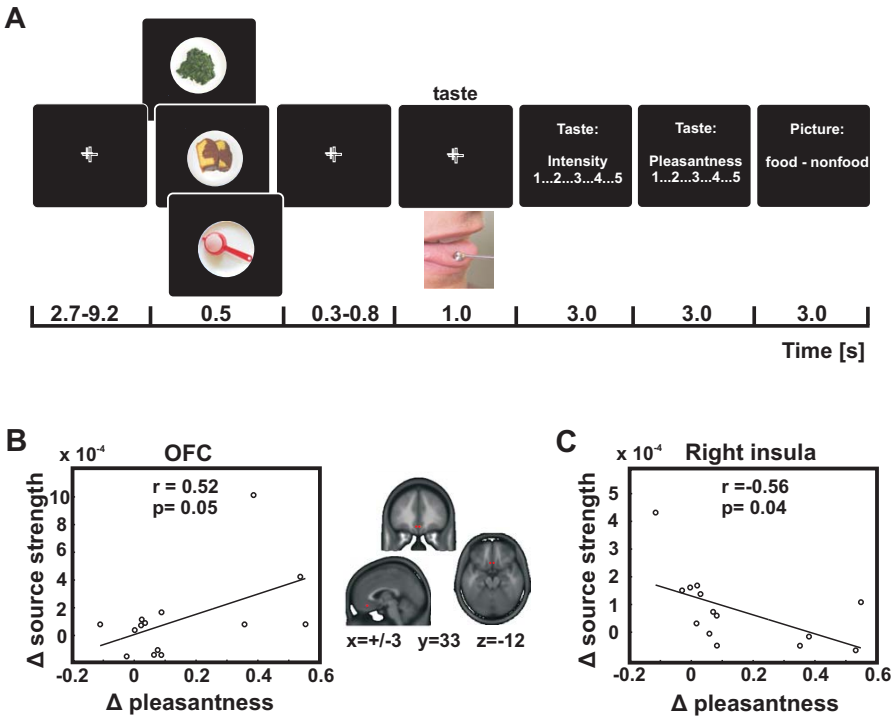

Figure 4: A: Experimental design. Each trial started with the presentation of a fixation cross followed by an image of either a high-calorie or a low-calorie food or a non-food item. Following a variable inter-stimulus interval, a neutral taste stimulus was presented. After the offset of the taste, participants had to first rate the taste intensity and pleasantness and then categorize the image preceding the taste into food vs. non-food items. They were naıve as to the task-irrelevant, i.e., high- and low-calorie image categories. (B) To illustrate the variety of high-calorie stimuli (160–717 kcal/100 g) and low-calorie stimuli (12–151 kcal/100 g), four pictures of each category are presented. High-calorie: Lamb-chops, Salmon, Pizza, Pastry. Low-calorie: Beans, Water melon, Yoghurt, Pasta w. Tomato Sauce. B and C: Correlations between changes in source strength and taste pleasantness ratings. Correlations were determined between changes in brain activation (i.e., high-calorie minus low-calorie) in the orbitofrontal cortex (B) and right anterior insula (C) and changes in participant's taste ratings (i.e., high-calorie minus low-calorie). The source strength was determined at the voxel exhibiting the maximum activity within the region of interest for each participant during the 176–236 ms period for the orbitofrontal cortex and during the 357–500 ms period for the right insula. (Adapted from Ohla et al., 2012b).

and sensitivity. Disregarding these inter-individual differences, sweet taste is commonly appreciated while bitter taste is generally disliked. Newborns show already a clear preference for sweet taste and an aversion to bitters. While these preferences are likely evolutionarily grounded, ensuring supply with carbohydrates and energy and protecting from ingestion of potentially harmful substances, they vary with experience and allow a larger variety of foods to be ingested (Menella and Beauchamp, 1996). Systematic manipulation of taste hedonics can utilize inter-individual differences in taste preferences and compare participants who "like" with those who "dislike" a given tastant (Rudenga and Small, 2013).

Alternatively, taste hedonics can be influenced by implicit or explicit cues similarly to visually presented foods (see Section 3.2. Ohla et al. (2012b) employed task-irrelevant visual food cues of either high- or low-energetic foods preceding a taste stimulus that was kept constant throughout the experiment (Figure 4 A). At the behavioral level, the identical taste stimulus was perceived as more pleasant when preceded by the image of a high-fat as opposed to a low-fat food. The effects are not surprising in light of cross-modal expectation-based modulation of taste perception (e.g., Nitschke et al., 2006). The mere viewing of food cues has been shown to activate brain areas associated with food perception and reward

(Killgore et al., 2003). Similarly, taste imagery (Kobayashi et al., 2004) or directing attention to taste even in its absence (Veldhuizen et al., 2007) activates the gustatory cortex. It is therefore not surprising that food images can elicit expectations about an imminent taste and that expectations about a taste, in turn, modulate activity in the insula (Nitschke et al., 2006; Veldhuizen et al., 2011b). Changes in pleasantness ratings observed by Ohla et al. (2012b) correlated positively with the neural source strength estimated for the N1 component at 180 ms after taste onset in the orbitofrontal cortex an area that has been related to taste hedonic processing in general but also when induced through verbal labels (Grabenhorst and Rolls, 2008). Negative associations were found between changes in pleasantness ratings and activation during the late positive component at 350ms in the right insula (Figure 4) which has been shown to respond to unpleasant taste an changes thereof (Nitschke et al., 2006). Why did the authors chose electric taste rather than a more food-related taste like sweet or salty? Most importantly, electric taste is typically not associated with any food, therefore, it allows to measure effects of visual food cues without confounding visual-gustatory associations as they exist for basic tastes. Moreover, it is neutral with respect to pleasantness and, hence, allows to measure changes in pleasantness in both direction along the scale. Together the study highlights that external cues modulate taste valuation and that these processes occur in a dynamic manner at early and later levels of stimulus processing in the brain. Although not reflected in the literature, the integration of sensory as well as sensory with conceptual information is crucial for food perception as it shapes subsequent food perception and choice. Predictive contextual cues influence perception of subsequent events through the elicitation of expectations about upcoming sensory events, which in turn bias perception toward the anticipated events and sharpen or enhance their perception when expectations are met (Engel et al., 2001). Yet, the question remains whether the findings reported by Ohla et al. (2012b) can be transferred to tastes of nutritional relevance such as sweet or salty, as electric taste bear very limited relevance for food perception. As the next step researchers should compare the potency of expectations induced by labels on tastes and flavors of individually preferred and unpreferred foods. Veldhuizen et al. (2011b) showed for the first time the neural networks involved when expectations about an imminent taste are breached by providing either the correct or false label for a sweet or a tasteless solution. Particularly attentional, reward-related, and primary taste areas responded to breaches of expectancy. Seubert and Ohla (2012) noted that "these findings are of high ecological relevance given that under real life conditions, the ingestion of a spoiled or novel food would often be the cause of a breach of expectancy reaction." (p. 1919).

5 Food flavor

Despite the recent premise that human noses can detect over 1 Trillion odors (Bushdid et al., 2014) and in contrast to visual impressions, odors are naturally ambiguous and the identification of an odor object heavily relies on input from other sensory channels or contextual information. Imagine the smell of cheese, in your favorite cheese store or a gym locker room - the same odor can likewise lead to the perception of a palatable food or repellent dirty socks depending on the context in which it is encountered.

Over 100 years after Henning (1916) first categorized odors into six basic odor qualities based on the verbal reports of human observers, many physiological or stimulus-centered approaches followed (Wise et al., 2000) and raised doubts on the reliability of Henning's approach. Until today, researchers have not yet found a categorical system incorporating stimulus properties, physiological binding action,

perception and inter-individual differences (see Kaeppler and Mueller (2013)). Odor perception and identification has been shown to improve by learning (Li et al., 2008) but also by contextual information from images (Gottfried and Dolan, 2003), tastes (Seo et al., 2013), sounds (Seo et al., 2014), color (Morrot et al., 2001) or labels (Bensafi et al., 2007). While trained individuals like someliers are skillful in odor categorization, at least for a particular subset of (trained) odors, the average person exhibits a rather rudimentary olfactory categorization expertise (Marino-Sanchez et al., 2010). Interestingly, it has been suggested that the superior odor identification and classification of wine experts is due to lesser susceptibility to semantic overshadowing, that is interference between odor and language processing (Lorig, 1999), rather than due to superior sensory sensitivity in experts compared to novices (Parr et al., 2002). Notably, the perception of an odor can even be transformed from the delicious odor of *parmesan cheese* to the aversive odor of *vomit* through mere provision of verbal labels for one or the other (Herz and von Clef, 2001) indicating profound susceptibility of odor identification to contextual information.

In the food context, smell and taste are closely intertwined and often even inseparable. Smell, undoubtedly, constitutes an eminent and potent sensory food attribute, which is usually encountered twice during eating. Smell is first perceived before ingestion, when sampling a food or beverage through orthonasal olfaction as part of the anticipatory phase of food perception. The second encounter of a food odor takes place during mastication through retronasal olfaction as part of the consummatory phase. Here, mastication of the food releases aroma compounds, odorous volatiles, which, after swallowing the first bite, travel from the mouth to the olfactory epithelium through the pharynx. During ingestion, the initially separate sensations of smell and taste merge toward a combined sensory experience commonly referred to as *flavor* (Verhagen and Engelen, 2006; Small, 2012). Because the neural mechanisms of multisensory integration have been derived almost exclusively from non-chemical senses it remains unclear whether common principles of multisensory integration (Stein and Meredith, 1990, 1993) provide the foundation of the merging of taste and smell. Yet, in line with the notion of superadditivity as a criterion for multisensory integration (Meredith and Stein (1983), but see Stanford and Stein (2007)), the flavor experience, as smell and taste merge, typically exceeds the sum of the two chemosensory modalities, resulting in a more object- or *Gestalt*-like, intense and rewarding sensory experience. Odors, despite their ambiguity, have been shown to enhance taste perception; for example strawberry and soy sauce odors, smelled or imagined, enhanced the sweet and salty taste of water-based solutions, respectively (Djordjevic et al., 2004).

Until now, only comparably few studies have investigated the integration mechanisms between smell and taste (Small and Prescott, 2005). In line with findings of anatomical connections between the primary gustatory and olfactory cortices (Rolls and Baylis, 1994; Shepherd, 2006), neuroimaging studies have reported convergence areas that respond to both, smell and taste, in the orbitofrontal cortex (de Araujo et al., 2003b; Rolls, 2004; Zald et al., 1998), the anterior insula, and frontal and parietal opercula (Cerf-Ducastel and Murphy, 2001; Small et al., 1999) as well as the primary olfactory cortex (Small et al., 2013, see). Less explored remains the neural basis for the emergence of the unique perceptual flavor experience. Only recently, commonalities and differences in brain networks when viewing, tasting and smelling food have been reviewed (Huerta et al., 2014). All three sensory modalities yielded responses in varying brain areas known as primary and associative cortices for the respective sensory modality as well as convergent activation of the (left anterior) insula. In particular, direct comparisons of activity associated with unisensory and multisensory input have consistently yielded effects in the rolandic

operculum and dorsal insular cortex (de Araujo et al., 2003b; Small et al., 2004). The insula has, in fact, been proposed as multisensory processing hub for chemosensory inputs from olfactory and gustatory stimuli (Veldhuizen et al., 2011a; de Araujo et al., 2003b), oral temperature (Guest et al., 2007), texture and fat (de Araujo and Rolls, 2004) but also for other, food-related percepts.

In an attempt to dissociate convergent areas that respond to odor, taste and *sub*additive flavor from areas showing *super*additive responses to flavor, (Seubert et al., 2015) used functional magnetic resonance imaging (fMRI) to compare the cortical processing of unisensory olfactory and gustatory stimulation of a familiar beverage (orange juice) to the combined olfactory–gustatory stimulation that emerges during its consumption, i.e., after swallowing. Convergent activations to chemosensory stimulation from the taste, the orthonasal smell as well as the flavor were observed in chemosensory association areas including the medial orbitofrontal cortex, the anterior insula, the superior frontal gyrus, and the parietal operculum and the lateral hypothalamus (Figure 5, right panel), the latter likely representing the appetitive value of these stimuli (Petrovich et al., 2005; Volkow et al., 2011). Within these convergent areas, *super*additive flavor activation, that is flavor activation exceeding the sum of activations to its unimodal constituents, was observed in the frontal operculum, an area that has been shown to respond not only to perceptual stimulus properties, but also to encode the reward value of the consumed item (Small et al., 2001; Stice et al., 2011). Within this network of cortical areas, the frontal operculum was coupled with both, sensory areas and higher order cognitive areas during the flavor perception, suggesting that it plays a central role in flavor formation. In particular, activity in the frontal operculum interacted with activity in the anterior insula, a gustatory area, and in the lateral entorhinal cortex, a relay to memory structures and central node for contextual modulation of odor processing. The increased connections between the frontal operculum and medial temporal memory structures during combined olfactory-gustatory stimulation point to a potential mechanism underlying the acquisition and modification of flavor preferences. Notably, areas commonly associated with multisensory integration, such as the superior temporal and middle frontal gyri and the intraparietal sulcus (Driver and Noesselt, 2008) exhibited superadditive activations that were driven by deactivations for the unimodal conditions (Figure 5, left panel).

Together, these findings suggest that the flavor percept from combined, congruent olfactory–gustatory stimulation is generated through superadditive activation of a distributed network comprising cortical areas that have been previously implicated in chemosensory as well as multisensory processing. Whether the increased neural coupling between the frontal operculum and medial temporal structures underlies the formation of flavor preferences and should be explored by future studies also with respect to its relevance for the formation of maladaptive food intake behavior.

6 Summary and Conclusion

In the chapters above, I presented a series of studies aiming to elucidate the cortical representations of the visual, gustatory and flavor components of food objects along with evidence for the vulnerability of these presentations to contextual information.

In CHAPTER 3, I introduced the role of food viewing as a convenient and valid means to investigate normal and deviant food perception and attitudes toward food (Blechert et al., 2010; Bohon et al., 2009; Nijs and Franken, 2012; Toepel et al., 2012). Most importantly, tasks involving food images have been

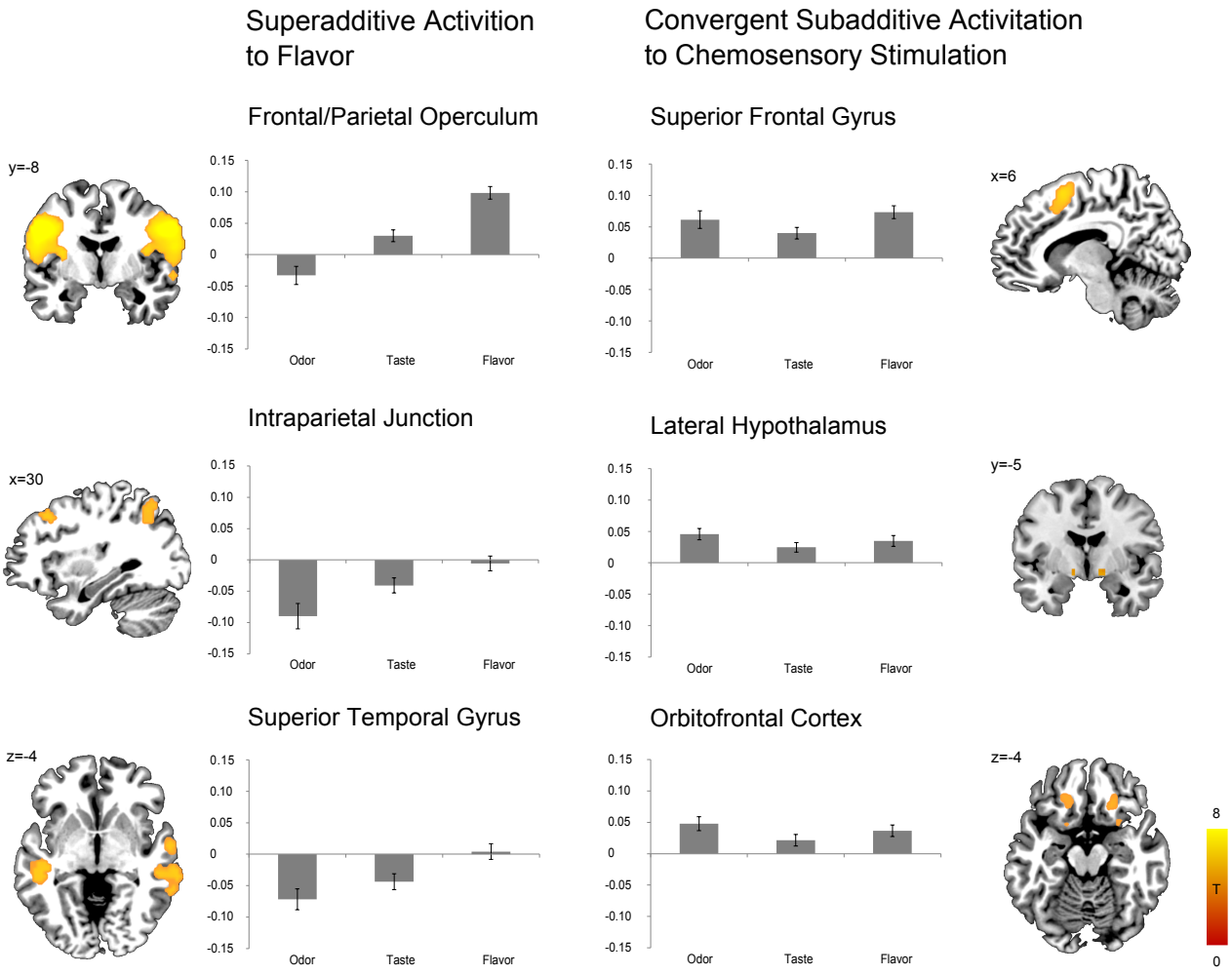

Figure 5: Superadditive activity to flavors (left) and convergent, but subadditive activation to all presentation modalities (right). Images are thresholded at 0.001 uncorrected for illustration purposes; the orbitofrontal cluster is thresholded at 0.05 uncorrected. Bar charts depict percent signal change relative to the modality-specific baseline. Error bars indicate standard error of the mean. (Reproduced from Seubert et al., 2015).

used to train eating control (van Koningsbruggen et al., 2014) and may, therefore, bear the potential to be implemented in portable training applications to improve dietary behavior. I, furthermore, emphasized the importance to control visual stimulus material with respect to both, physical stimulus features and subjective perception, in studies of visual food processing, partially because these two dimensions are not independent (see Meindl and Ohla, 2015). While this requirement may appear self-evident it has not always been pursued with desirable perseverance in food viewing experiments. Our presented image database (Blechert et al., 2014) comprising of food, food-related and non-food control images grants researchers access to high-quality photographs along with relevant physical properties and subjective ratings to conduct controlled and replicable studies. However, food perception is not only influenced by physical food attributes but also by information from implicit and explicit external cues. Verbal labels as an integral part of food packages and advertisements have been shown to influence the perception and valuation food stimuli and decision-making (e.g., Grabenhorst and Rolls, 2008; Linder et al., 2010). Toepel et al. (2014) investigated at which level of the food perception pathway, at early, sensory or later, evaluative levels, verbal labels act. We found that visually presented high-energy foods yielded reduced activity in brain areas associated with cognitive control and goal-adaptive behavior when preceded by positive compared to neutral or negative verbal labels. The findings suggest that positive labels reduce cognitive control and increase valuation of the high-energy foods in the absence of effects on sensory processing. Whether the observed effects translate to subjective experiences of pleasure or even behavior such as overconsumption of high-energy foods remains to be elucidated.

In CHAPTER 4, I presented insights into the temporo-spatial dynamics of taste processing, that is the sense that is mediated by dedicated gustatory receptors on the tongue. Despite decades of research, the workings by which the peripheral taste signal is used by the human central nervous system to encode taste is only beginning to be understood. This is due, in part, to the fact that chemical stimuli delivered into the mouth are difficult to control with respect to their physical properties, i.e., place of stimulation and onset/offset. Most of our current understanding of the cortical areas involved in human taste perception has been derived from neuroimaging techniques which are relatively forgiving to imprecise stimulus onset such as functional magnetic resonance imaging (fMRI) or positron emission tomography (PET). We have conducted a series of studies to characterize the morphology and time course of the gustatory event-related potential and to estimate its cortical generators (Ohla et al., 2009, 2010, 2012a). One aspect in which taste differs from other senses is the categorical structure of gustatory phenomenology. For example, we could describe our phenomenology of having a cup of coffee as “I see the cup”, and “it smells like coffee”, and “it tastes bitter”. Thus, when we describe our perception in other senses, we usually refer to the object evoking this perception, but we describe taste only with a categorical or quality label. Therefore, one of the most pertinent research questions in taste research is to clarify how taste qualities are represented in the human brain and whether this information is used for decision-making. Using multivariate pattern classification (decoding) of the EEG signal obtained during tasting different tastes, we could show that different tastes evoke different dynamic patters of electrical activity and that the onset of this decoding coincided with the earliest taste-evoked responses, within only 175 ms, suggesting that quality is among the first attributes of a taste represented in the central gustatory system (Crouzet et al., 2015). Moreover, we provided evidence for a neural-phenomenological mapping for taste quality, that is a correlation between the neural pattern and subjective quality experience (Crouzet et al., 2015).

Taste hedonics represent another feature describing taste which is tightly linked with other attributes such as the intensity, quality and familiarity of a taste. In order to investigate the neural underpinning of taste pleasantness independent of other taste features, we employed a crossmodal visual-gustatory cueing task with either high-caloric, low-caloric food or non-food images preceding a neutral taste (Ohla et al., 2012b). At the same time, this paradigm illustrates the vulnerability of taste perception to contextual information and the expectations thereof (Seubert and Ohla, 2012). We observed increased pleasantness ratings associated with increased activity in orbitofrontal cortex, which is know to participate in taste hedonic processing, and down-regulation of the right insula, which can be interpreted as an inhibition of unpleasant experiences (Ohla et al., 2012b). Future studies will have to test whether the findings generalize to tastes of nutritional relevance such as sweet or salty and whether external cues (e.g., images or labels) can be utilized to influence food acceptance and preference at an individual level.

In CHAPTER 5, I reviewed the anatomical substrate contributing to flavor perception from the simultaneous experience of taste and smell during consumption. While the merging of taste and smell is of high ecological relevance, relatively little is known about the underlying mechanisms. We addressed whether flavor of a familiar beverage is perceived and processed differently from its components, taste and smell alone. When comparing brain activity to the odor, the taste and the odor-taste combination, we found convergent activations in chemosensory association areas (Seubert et al., 2015). Notably, superadditive activity, that is flavor activation exceeding the sum of activations to taste and smell alone, was observed only in the frontal operculum, which presumably plays a key role in flavor formation as it was, furthermore, coupled with other sensory and higher cognitive areas. The results evidence that flavor is generated in a distributed network comprising chemosensory, reward-related as well as multisensory brain areas. Next, activity patterns within this network should be investigated with respect to individual differences in flavor preference and maladaptive food intake behavior .

Together, I reckon that an understanding of the psychophysiological mechanisms of the sensory and affective processing of food objects mediated by our senses, seeing, smelling, tasting, feeling and hearing, represents the perceptual basis of food-related decision making. It will enable further investigations of the mechanisms by which internal and external factors, such as attitudes or individual experiences and labels, respectively, influence food perception, valuation and, eventually, intake behavior. Unraveling the workings of food sensory perception and gratification are critical to tackle deviant eating behavior and to reduce detrimental health consequences for individuals in the long run.

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8 Appendices

8.1 Declaration of authorship

Hiermit erkläre ich, dass die unter meinem Namen vorgelegte Habilitationsschrift unter Berücksichtigung der dargelegten Koautorenkontributionen eigenständig von mir verfasst worden ist.

Dr. Kathrin Ohla

8.2 Publications

Crouzet SM, Busch NA, **Ohla K** (2015). *Taste quality decoding parallels taste sensations.* **Current Biology**. 25(7):890-896

Seubert J, **Ohla K**, Yokomukai Y, Kellermann T, Lundström JN (2015). *Superadditive opercular activation to food flavor is mediated by enhanced temporal and limbic coupling*. **Human Brain Mapping**, 36(5):1662-76

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